In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1264V

Filed: December 7, 2023

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JUDITH WILSON

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* *

Ronald Homer and Meredith Daniels, Conway, Homer, P.C., Boston, MA, for Petitioner
Nina Ren, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On September 15, 2017, Judith Wilson ("Petitioner"), filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program") alleging that she developed rheumatoid arthritis ("RA") as a result of the influenza vaccination she received on October 13, 2015. Pet. at 1. For the reasons discussed in this decision, I find that Petitioner has not demonstrated that that the flu vaccine can cause or did cause her condition.

[1] Because this Decision contains a reasoned explanation for the action in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

I. Procedural History

Petitioner filed her petition on September 15, 2017, alleging that she developed RA from the influenza vaccination she received on October 13, 2015. Pet. at 1.

Petitioner filed medical records on September 21, 2017. Exs. 1-8; ECF No. 7. On July 19, 2018, Respondent filed a Rule 4(c) Report stating Petitioner has not met her burden of proving entitlement to compensation under the Vaccine Act. Resp't's Rep. at 11; ECF No. 23.

The parties then filed expert reports from their respective expert rheumatologists: Dr. Kristin Gowin for Petitioner and Dr. Mehrdad Matloubian for Respondent. Exs. 15, 17, 25, A, C, D.

Petitioner filed an amended petition on August 9, 2022. In it, she clarified "in the event that the Court finds that petitioner's RA was pre-clinical prior to her October 13, 2015, flu vaccination, the petitioner alleges, in the alternative, that the aforementioned flu vaccination resulted in a significant aggravation of her previously pre-clinical RA." Amended Pet. at 2; ECF No. 60.[3]

I held an entitlement hearing on August 23, 2022. After the hearing, the parties filed post-hearing briefs. ECF Nos. 63, 64, 65. This matter is now ripe for an adjudication.

II. Medical Records

A. Relevant Pre-Vaccination History

Petitioner's medical history is not in dispute. Her pre-vaccination history is remarkable for breast cancer requiring a left mastectomy, obesity, asthma, scoliosis, obstructive sleep apnea, irritable bowel syndrome, and arthritis of the left wrist. Ex. 5 at 71, 129, 421; Ex. 7 at 11-12.[4] Petitioner smoked approximately 0.8 packs of cigarettes per day from 1971 to 1986. Ex. 6 at 3. She received several vaccinations prior to the allegedly causal one here without incident. *See* Ex. 1 at 1.

On January 10, 2013, Petitioner saw Mary Flynn, M.D., and reported muscle pain, chills, headache, and a cough, and was diagnosed with "likely influenza." Ex. 5 at 22. On January 25, Petitioner reported low energy level for the past ten years and lower left quadrant pain since September 2012. *Id.* at 71. Dr. Flynn ordered labs, including erythrocyte sedimentation rate ("ESR")[5], which were normal. Ex. 8 at 20-22.

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[3] The analysis of the claim through the lens of causation-in-fact versus significant aggravation does not change the result. The same points that prevent Petitioner from prevailing in a causation-in-fact analysis also undermine a significant aggravation claim. As a result, I have not conducted a significant aggravation analysis.

[4] Throughout this Decision, citations to specific pages in medical record exhibits refer to the page numbers printed at the bottom of each page rather than the page number in the PDF viewer.

On May 31, 2013, Petitioner saw her primary care provider ("PCP"), Melissa Grimm, M.D. Ex. 5 at 133. Petitioner reported that her right knee had felt swollen, tight, and painful, since May 17, but that she did not recall a specific injury. *Id.* Examination revealed decreased range of motion on flexion and a small effusion.[6] *Id.* at 136. The differential diagnosis included "possible meniscal tear or other internal derangement vs tendonitis/anserine bursitis[7] (though location not typical)." *Id.* Dr. Grimm recommended physical therapy ("PT"). *Id.*

Petitioner underwent an MRI of her right knee on June 5, 2013, which revealed a small tear in the medial meniscus, articular cartilage loss of the patella, and a small effusion. Ex. 13 at 57.

Petitioner saw her oncologist in October 2013 for left arm pain that she believed was related to her left mastectomy. Ex. 6 at 19. Her oncologist's assessment was left shoulder pain with limited range of motion, "[l]ikely related to prior breast surgery." *Id.* She recommended occupational therapy ("OT"). *Id.*

B. Post-Vaccination History

Petitioner received the allegedly causal flu vaccine in her right arm on October 13, 2015 when she was 61 years old. Ex. 5 at 421; Ex. 1 at 1.

On October 26, 2015, Petitioner underwent an OT evaluation for stiffness in her left shoulder and chest and an adherent scar. Ex. 6 at 72. The occupational therapist noted normal range of motion in both shoulders and recommended continuing OT. *Id.* at 73. At a follow-up OT appointment on November 2, 2015, there is no documentation of pain in Petitioner's right shoulder or other joints. *Id.* at 79-80.

On November 16, 2015, Petitioner called the nurse line at Unity Point Health – Meriter complaining of right shoulder and arm pain that felt "like rotary cuff" for about one week. Ex. 8 at 61-62. She stated that she had had this problem in the past and requested a referral to PT, which was provided. *Id.*

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[5] ESR is "the rate at which erythrocytes precipitate out from a well-mixed specimen of venous blood…an increase in rate is usually due to elevated levels of plasma proteins…It is increased in monoclonal gammopathy, hypergammaglobulinemia due to inflammatory disease, hyperfibrinogenemia, active inflammatory disease, and anemia." DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition? id=102146 (last visited Nov. 29, 2023) (hereinafter "DORLAND'S").

[6] Effusion is "the escape of fluid into a part or tissue." DORLAND'S, https://www.dorlandsonline.com /dorland/definition?id=15649 (last visited Nov. 30, 2023).

[7] Anserine bursitis "inflammation of the anserine bursa with pain on the medial side of the knee, sometimes seen after jogging or other heavy knee exercise and in heavy individuals with genu valgum [commonly known as 'knock knee']." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=62215 (last visited Nov. 30, 2023).

Petitioner underwent a PT evaluation on November 17, 2015. Ex. 4 at 3-5. Petitioner reported that she had been awakened in the middle of the night by right shoulder pain on November 9. *Id.* at 3. Her pain was in the front of her right shoulder, radiated down the side of her shoulder and elbow to her wrist, and worsened with shoulder movement. *Id.* Examination revealed limited and painful range of motion in the right shoulder and positive impingement tests. *Id.* The physical therapist's impression was that Petitioner's symptoms were "consistent with right subacromial bursitis and shoulder impingement." *Id.* at 5. Petitioner's right shoulder pain improved over the next few weeks with additional PT and application of ice. Ex. 6 at 85; Ex. 4 at 29.

At a PT appointment on December 3, 2015, Petitioner stated that her right shoulder was doing better, but complained of bilateral hand and finger pain and swelling of the left hand. Ex. 4 at 47. Examination confirmed moderate swelling in the left hand and fingers. *Id.* Petitioner reported these symptoms to Dr. Grimm on December 4, who noted swelling in Petitioner's hands "with slight evidence of tenosynovitis[8]," of the hands and fingers, and swelling of the legs. *Id.* at 443. Dr. Grimm suspected post viral reactive arthritis, polyarthralgia, and tenosynovitis of the finger and hand. *Id.* 446. She prescribed prednisone and ordered blood work that revealed elevated ESR and C-reactive protein ("CRP")[9]. *Id.; id* at 440-41.

Petitioner saw her gynecologist on December 17, 2015, at which she reported that since taking prednisone, she had "never felt this good for [five] years!" Ex. 2 at 22. She reported that her aches and pains were gone, and her energy level was up. *Id.* She also reported that her pain was returning with the tapering of prednisone use. *Id.* Petitioner had felt fatigue for several years, which she attributed to her sleep apnea, and her gynecologist recommended following up with a rheumatologist to address the underlying autoimmune condition. *Id.* Petitioner also reported that the prednisone made her feel better than she had in five years at her PT appointment on December 18. Ex. 4 at 67.

On January 21, 2016, Petitioner saw rheumatologist Christine Sharkey, M.D. Ex. 5 at 463. On examination, Dr. Sharkey noted tenderness in Petitioner's neck, shoulders, feet, and tenderness and swelling in the metacarpophalangeal joints of both hands. *Id.* at 466. Dr. Sharkey ordered lab work and x-rays of Petitioner's hands, feet, and ankles. *Id.* at 467. The results revealed elevated CCP and rheumatoid factor ("RF")[10]. *Id.* at 492-94. Dr. Sharkey diagnosed Petitioner with rheumatoid arthritis ("RA"). *Id.* at 497.

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[8] Tenosynovitis is "inflammation of a tendon sheath." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=49214 (last visited Nov. 30, 2023).

[9] The acute phase of the immune response is "a group of physiologic processes occurring soon after the onset of infection, trauma, inflammatory processes, and some malignant conditions. The most prominent change is a dramatic increase of acute phase proteins, especially C-reactive protein, in the serum. Also seen are fever, increased vascular permeability, and a variety of metabolic and pathologic changes." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=103669 (last visited Nov. 30, 2023) (emphasis added).

[10] RF or rheumatoid factor is "antibodies directed against antigenic determinants…these are found in the serum of about 80 percent of persons with classical or definite rheumatoid arthritis." DORLAND'S, https://www. dorlandsonline.com/dorland/definition?id=74591 (last visited Nov. 30, 2023).

Petitioner's January 21 x-rays showed mild osteoarthritis in her hands and no sign of arthritis in her feet. Ex. 7 at 7-9. Petitioner underwent an MRI of her right hand on February 25, 2016. Ex. 13 at 45. The results showed "mild synovial enhancement" and "[m]inor degenerative changes" at the first carpometacarpal joint, without erosions. *Id.* "Mild tenosynovitis of the flexor tendons of the 3rd and 5th fingers as well as the flexor pollicis longus" was also noted. *Id.*

Petitioner returned to Dr. Sharkey on March 4, 2016. Ex. 5 at 529. Dr. Sharkey noted that Petitioner's lab and imaging results were consistent with seropositive RA. *Id.* at 532. She prescribed methotrexate and renewed Petitioner's prednisone prescription. *Id.* Petitioner also received a pneumococcal vaccination. *Id.*

Petitioner filed many more records documenting her treatment for RA. *See, generally,* Exs. 5, 7, 12, 30. On March 2, 2017, Petitioner stated that she was "doing very well" with medication. Ex. 8 at 134. At an appointment on June 16, 2017, Dr. Sharkey noted that Petitioner had full range of motion in her neck, temporomandibular joint, shoulder, elbows, wrist, small joints of her hands, and ankles. Ex. 12 at 256. Petitioner has been receiving medication intravenously once or twice a week since her diagnosis. Ex. 30 at 66-69, 210-14, 369-73, 1020-24. In May 2022, Petitioner experienced a symptom flare that resolved with a prednisone taper. *Id.* at 44-50.

No other pertinent medical records have been filed.

III. Petitioner's Affidavit

Petitioner signed her affidavit on September 15, 2017. Ex. 9 at 8. In it, she averred that she was generally healthy, although noted that she received a breast cancer diagnosis in 2010 which was treated with a mastectomy. *Id.* at 1. Petitioner received a flu vaccine on October 13, 2015, and noticed some physical changes within the next week that concerned her. *Id.* at 2. Petitioner described that she went on vacation to Florida during this timeframe, and stated that she felt "weak, was hot and sweaty, fatigued, and experienced shortness of breath with little exertion." *Id.* The symptoms persisted for the week that she was in Florida. *Id.*

Upon returning home from Florida, Petitioner stated that she began to experience pain in her right shoulder. Ex. 9 at 2. She took some over-the-counter pain medication, but that did not help. *Id.* Petitioner described that on October 26, 2015, she had a follow-up OT appointment for her mastectomy. *Id.* She was very fatigued on the day of this appointment, and asked her husband to use the valet parking. *Id.* Because the valet parking was closed, they had to park in the parking lot. *Id.* Petitioner described the walk to the hospital: "I remember trying to walk from my car to the elevator in the parking ramp and forgetting to take my parking ticket. I had to walk back to the car to get it and was so exhausted I wanted to cry." *Id.* at 2-3.

Petitioner stated that during November 2015, she continued to experience shoulder pain, and noted that the pain also began to involve her right elbow and right wrist. Ex. 9 at 3. This progressed to involve the joints in both hands and her jaw. *Id.* at 3-4. Petitioner visited a doctor who prescribed prednisone. *Id.* at 4. This treatment helped, but it did not decrease the swelling in her hands. *Id.*

In January of 2016, Petitioner saw a rheumatologist, Dr. Sharkey, who diagnosed her with RA. Ex. 9 at 5. Dr. Sharkey started her on methotrexate injections and continued prednisone. *Id.*

As of the date she signed her affidavit, Petitioner's RA has impacted her daily life. Ex. 9 at 7-8. She cannot safely get in and out of the bathtub and cannot wash her own hair. *Id.* at 7. She cannot perform housework, cannot walk the dog, and sometimes cannot drive. *Id.* at 7-8.

IV. Expert Opinions and Qualifications

A. Petitioner's Expert: Dr. Kristin Gowin, M.D.

1. Qualifications

Dr. Kristin Gowin attended Miami University in Ohio, and received a Bachelor of Arts Degree in Zoology. Ex. 16 at 1 (hereinafter "Gowin CV"). She received her M.D. from the University of Cincinnati College of Medicine and completed her residency in internal medicine at the Milton S. Hershey Medical Center. *Id.* at 1-2. Dr. Gowin attended the University of Pennsylvania School of Medicine and received a Master of Science in Clinical Epidemiology ("MSCE"). *Id.* at 1. She served as a Faculty Fellow at the University of Pennsylvania School of Medicine, Center for Clinical Epidemiology and Biostatistics, from 1997 to 1999, and was additionally a Fellow in the Division of Rheumatology from 1994 to 1998. *Id.*

Dr. Gowin was appointed as Instructor in Medicine at the Milton S. Hershey Medical Center from 1993 to 1994, served as an attending physician in rheumatology at the Philadelphia Veterans Affairs Medical Center from 1997 to 1999, and also served as an instructor in the division of rheumatology at the Hospital of the University of Pennsylvania from 1998 to 1999. *Id.* at 2. She is currently a partner at the Asheville Arthritis and Osteoporosis Center where she actively follows approximately 1,000 patients. Tr. at 7. Dr. Gowin is board certified in rheumatology. *Id.* I recognized her as an expert in rheumatology and clinical epidemiology. *Id.* at 9.

2. Expert Reports and Testimony

Dr. Gowin filed three expert reports in this case. Exs. 15 (hereinafter "First Gowin Rep."), 17 (hereinafter "Second Gowin Rep."), 25 (hereinafter "Third Gowin Rep."). She also testified at the entitlement hearing.

Dr. Gowin stated that Petitioner met the diagnostic criteria for RA at the time of her initial rheumatology evaluation. First Gowin Rep. at 9. During that appointment, she had more than 10 tender and swollen joints, she had been symptomatic for more than six weeks, and she had elevation of inflammatory markers, to include rheumatoid factor, anti-CCP, erythrocyte sedimentation rate, and C-reactive protein. *Id.*

During the entitlement hearing and in her expert reports, Dr. Gorwin supported her position that the flu vaccine can cause RA through various case reports and other articles.[11]

Dr. Gowin discussed the Herron article. Tr. at 17-18. Anne Herron et al., *Influenza Vaccination in Patients with Rheumatic Diseases Safety and Efficacy,* 242 J. AM. MED. ASSN. 53-56 (1979) (filed as Ex. 15, Tab D) (hereinafter "Herron"). In this 1979 article, doctors looked at rheumatology patients to see if the flu vaccine could cause autoimmune flares. The authors concluded that flu vaccine is generally safe, however 6/17 RA patients had disease flares. Herron at 55.

Dr. Gowin also testified about the Basra article. Tr. at 16. Gurjot Basra et al., *Rheumatoid Arthritis and Swine Influenza Vaccine: A Case Report*, CASE REPORTS IN RHEUMATOLOGY, Vol. 2012, doi:10.1155/2012/785028 (filed as Ex. 24) (hereinafter "Basra"). Basra is a case report which describes a patient who developed RA one month after an H1N1 vaccination.

Concerning a causal theory, Dr. Gowin opined "there is biologic plausibility for the influenza vaccine to cause either onset or flare of RA." First Gowin Rep. at 9. She proposed that the vaccine initiates the activation of T-lymphocytes. *Id.* Though no single driving antigen has been identified, there may be several that initiate RA in genetically susceptible individuals via the mechanism of molecular mimicry. *Id.* (citing Peter Schur et al., *Pathogenesis of rheumatoid arthritis*, Up-to-date 2012 at 1 (filed as Ex. 15, Tab G) (hereinafter "Schur")). "The activation of the immune cascade causes ingrowth of blood vessels, recruitment of further immune cells that produce antibodies like the classic RA factor and anti-CCP and proliferation of the lining of the joint (synovium) that eventually causes damages to the cartilage." First Gowin Rep. at 9.

Dr. Gowin testified that the causation theory she has offered in this case is not specific to the flu vaccine. She testified that any vaccine could behave in a similar manner and either cause or significantly aggravate RA. Tr. at 54-55.

When discussing molecular mimicry, Dr. Gowin was not able to identify a specific self-antigen that the flu vaccine was able to mimic and cause disease. Tr. at 55. She agreed that seropositive RA is generally not considered to be a post-infectious disease. *Id.* at 50. She testified that "there has not been a particular virus that's been implicated" in the pathogenesis of RA. *Id.* She further agreed on cross-examination that she had not been taught in her rheumatology training that influenza infection can trigger RA. *Id.* at 51.

I asked Dr. Gowin, "How does the flu vaccine cause [RA] via molecular mimicry if the virus isn't known to?" Tr. at 67. Dr. Gowin responded follows:

> So the vaccines are different. They modify pieces of virus, and they use adjuvants which make the immune system respond more to those pieces of the virus. So since it's not an intact virus, it may be that if you break down those specific pieces, that

[11] While I have considered them, I do not find case reports that discuss the development of conditions other than RA, such as vasculitis, reactive arthritis, and PMR, to be especially persuasive in demonstrating that the flu vaccine can cause RA.

> those would be more likely for your immune system to recognize that as a molecular mimic versus the entire virus.

Id.

Dr. Gowin noted that "molecular mimicry is not the only mechanism by which the influenza vaccine may have contributed to the onset of rheumatoid arthritis", conceding that "exact etiology and triggers for rheumatoid arthritis are not known." Second Gowin Rep. at 2. During the entitlement hearing, she mentioned immune cascade, where an antigen is taken up by an antigen presenting cell and then "interacts with lymphocytes, T lymphocytes and then B lymphocytes." Tr. at 22. The B lymphocytes produce antibodies and the T lymphocytes produce cytokines. *Id.* The production of cytokines results in the recruitment of other immune cells. *Id.* This leads to the formation of immune complexes, which Dr. Gowin defined as multiple antigen-antibody pairs binding together to form "clumps." *Id.* at 23. Dr. Gowin explained that if these immune complexes get big enough, the immune system can begin to see them as foreign and attack them. *Id.*

Dr. Gowin ultimately concluded that the flu vaccine caused Petitioner to develop RA. First Gowin Rep. at 9; Tr. at 39.

B. Respondent's Expert: Dr. Mehrdad Matloubian

1. Qualifications

Respondent offered the medical expert opinion of Dr. Mehrdad Matloubian. Dr. Matloubian is a physician and Associate Professor of Medicine in the division of rheumatology at the University of California, San Francisco. Ex. B at 1 (hereinafter "Matloubian CV"). He has been on faculty at UCSF for approximately 21 years. Matloubian CV at 2. Dr. Matloubian is a board-certified and practicing rheumatologist. *Id.*

Dr. Matloubian also has a Ph.D. in virology/immunology and has been engaged in research in this area for more than twenty years. *See generally*, Matloubian CV. His areas of expertise include T and B cell responses, especially to viruses as well as factors that regulate lymphocyte circulation and trafficking. *Id.* at 2-3. Throughout most of his research career, he has focused on innate and adaptive immune responses, including those of T and B cells, to acute and chronic viral infections. *Id.* at 6-7. Dr. Matloubian has published peer-reviewed articles in both areas. *Id.* at 8-11. Dr. Matloubian actively evaluates and treats patients with complex autoimmune diseases at a tertiary referral center and has a great interest in mechanisms of autoimmunity. Matloubian CV at 2. Tr. at 80. I recognized him as an expert in rheumatology and immunology. Tr. at 81.

2. Expert Reports and Testimony

Dr. Matloubian filed three expert reports in this case. Exs. A (hereinafter "First Matloubian Rep."), C (hereinafter "Second Matloubian Rep."), and D (hereinafter "Third Matloubian Rep."). He also testified at the entitlement hearing.

Dr. Matloubian opined that the pathogenesis of RA is not well understood, but that genetic and environmental factors are thought to play a role. First Matloubian Rep. at 7. He also opined that, in RA, the breakdown in immune tolerance and development of autoantibodies such as rheumatoid factor and anti-CCP antibodies "precede clinically apparent symptoms by several years." *Id.*

Dr. Matloubian stated that medical literature supports the idea that the RA disease course is divisible into multiple phases. First Matloubian Rep. at 7. One such model proposes six phases: (1) genetic risk factors; (2) environmental risk factors (e.g., smoking, antibiotics); (3) systemic autoimmunity; (4) clinical symptoms; (5) unclassified arthritis; and (6) RA. *Id.* (citing H.W. van Steenbergen et al., *The Preclinical Phase of Rheumatoid Arthritis: What is Acknowledged and What Needs to Be Assessed?*, 65(9) ARTHRITIS & RHEUMATISM 2219-32 (2013) (filed as Ex. A, Tab 11)). Dr. Matloubian opined that factors such as infections, toxins, drugs, and radiation may impact this progression in a particular patient, but that the long lag time between development of autoantibodies and clinical disease makes causation very difficult to establish. *Id.* at 8. Dr. Matloubian also opined that the apparent complexity of the pathogenesis of RA makes "simplistic explanations, such as molecular mimicry," less likely. *Id.* at 9.

Dr. Matloubian disagreed with Dr. Gowin's theory of molecular mimicry as the mechanism by which the flu vaccine can cause RA. First Matloubian Rep. at 13. He opined that, molecular mimicry "has rarely been persuasively demonstrated as the cause of autoimmunity in humans." *Id.* He further opined that in order for molecular mimicry to be relevant here, the natural flu infection should also cause RA in some patients, but it does not. *Id.*

Dr. Matloubian discussed his opinion that a history of smoking increases the risk of developing RA. First Matloubian Rep. at 8-9; Tr. at 86-90. He cited medical literature positing a link between smoking and citrullinated peptides that bind to HLAs and elevate the risk of RA. *Id.* at 88 (citing Vivianne Malmström et al., *The immunopathogenesis of seropositive rheumatoid arthritis: from triggering to targeting*, NATURE REVS.: IMMUNOLOGY 1-16 (2016) (filed as Ex. A, Tab 4)). He noted that Petitioner had a history of smoking. First Matloubian Rep. at 9.

Dr. Matloubian stated that, based on the literature, there is no link between viral vaccines and autoimmunity. First Matloubian Rep. at 12. He also opined that the flu vaccine is recommended for patients with RA. *Id.* at 15. He explained that this is so because RA patients are frequently prescribed immunosuppressant medications, making flu infection more dangerous. *Id.*

Dr. Matloubian testified about various studies concerning the flu vaccine and RA. He discussed Jasvinder A. Singh et al., *2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis*, ARTHRITIS & RHEUMATOLOGY, 1-25, 2015, (filed as Ex A, Tab 19) (hereinafter "Singh"). Dr. Matloubian testified that the American College of Rheumatology recommends that people with RA receive the flu vaccine. Tr. at 136.

Dr. Matloubian discussed the Bengtsson study. *See* Camilla Bengtsson et al., *Common vaccinations among adults do not increase the risk of developing rheumatoid arthritis: results from the Swedish EIRA study*, 69 ANNALS OF RHEUMATIC DISEASES 1831-33 (2010) (filed as Ex. A, Tab 16) (hereinafter "Bengtsson"). Bengtsson is a case-control study, which Dr. Matloubian

defined as a study with two populations, one with a disease and one without. According to Dr. Matloubian, the study found that "vaccinations did not increase the risk of RA overall." Tr. at 127. They controlled for genetic risk factors and for smoking. *Id.* at 127-28. Dr. Matloubian testified that the study is quite reliable. *Id.* at 128.

Dr. Matloubian also discussed Johanna Westra et al., *Vaccination of patients with autoimmune inflammatory rheumatic diseases*, 11 RHEUMATOLOGY 135-45 (2011) (filed as Ex A, Tab 17) (hereinafter "Westra"). Westra is a review of the safety of different types of vaccines in people with autoimmune rheumatic diseases. Tr. at 134. He testified the article concluded that RA patients do not experience a flare in their disease after flu vaccine. Tr. at 135; Westra at 140.

Dr. Matloubian testified that Petitioner's flu vaccine did not cause her to develop RA. Tr. at 99. He articulated several reasons for this opinion. Petitioner was at the peak age of onset of the disease; she was a prior smoker, which is the only established environmental risk factor for developing RA; despite millions of doses of the flu vaccine being administered worldwide, the vaccine is not associated with either onset of RA or RA flares; the flu vaccine is recommended for people with RA; influenza infection causes a lot more cytokines to be produced than the vaccine, yet there is no association between the influenza infection and RA. Tr. at 99-100.

V. Applicable Law

A. Petitioner's Burden

Under the Vaccine Act, when a petitioner suffers an alleged injury that is not listed in the Vaccine Injury Table, a petitioner may demonstrate that she suffered an "off-Table" injury. § 11(c)(1)(C)(ii).

In attempting to establish entitlement to a Vaccine Program award of compensation for an off-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioner establish by preponderant evidence that the vaccination she received caused her injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Under the first prong of *Althen*, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs*., 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Hum. Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing

Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325-26 (2007)). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360 (*quoting Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010)). Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs*., 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017); *see also Hock v. Sec'y of Health & Hum. Servs*., No. 17-168V, 2020 U.S. Claims LEXIS 2202 at *52 (Fed. Cl. Spec. Mstr. Sept. 30, 2020).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause-and-effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record. *Hibbard v. Sec'y of Health & Hum. Servs*., 100 Fed. Cl. 742, 749 (2011), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Hum. Servs*., No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs*., 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem*., 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs*., 3 F.3d 413, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records created contemporaneously with the events they describe are generally trustworthy because they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions," where "accuracy has an extra premium." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378 (Fed. Cir. 2021) citing *Cucuras*, 993 F.2d at 1528. This presumption is based on the linked proposition that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825 at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013), *claim den*., 2020 WL 5641872 (Fed. Cl. Spec. Mstr. Aug. 26, 2020), *rev. den.*, 152 Fed. Cl. 782 (2021), *rev'd and remanded*, 34 F.4th 1350 (Fed. Cir. 2022).

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475 at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony -- especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; see also *Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475 at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should

be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent and compelling." *Sanchez*, 2013 WL 1880825 at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90-2808V, 1998 WL 408611 at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), aff'd, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted").

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion

"connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations").

D. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VI. Analysis

Because Petitioner does not allege an injury listed on the Vaccine Injury Table, her claim is classified as "off-Table." As noted above, to prevail on an "off-Table" claim, Petitioner must prove by preponderant evidence that she suffered an injury and that this injury was caused by the vaccination at issue. *See Capizzano*, 440 F.3d at 1320.

A. Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic inflammatory disease that causes joint inflammation, pain, and degeneration. Daniel Aletaha et al., *2010 Rheumatoid Arthritis Classification Criteria, An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative*, 62(9) ARTHRITIS & RHEUMATISM 2569-81 (2010) (filed as Ex. 15, Tab H). Its pathogenesis is incompletely understood. First Matloubian Rep. at 7. If left untreated, RA leads to loss of physical function and ability to perform and carry out daily tasks. David L. Scott et al., *Rheumatoid arthritis*, 376 LANCET 1094-1108, 2010 (filed as Ex. A, Tab 12). RA is a disease that affects peripheral joints typically in the hands and feet. First Matloubian Rep. at 6. Two different type of RA include seropositive and seronegative RA. *See* Malmström at 1. Seropositive RA is the more common of the two, affecting two-thirds of the RA population. *Id.* In order to be classified as having seropositive RA, an individual has anti-CCP antibodies. Tr. at 84.

RA is a common rheumatologic disease that affects 3.6% of adults, 1 in 28 women and 1 in 59 men. First Matloubian Rep. at 6, citing Cynthia Crowson et al., *The Lifetime Risk of Adult-Onset Rheumatoid Arthritis and Other Inflammatory Autoimmune Rheumatic Diseases*, 63 ARTHRITIS & RHEUMATISM 3, 633-39 (2011) (filed as Ex. A, Tab 2). Peak onset of the disease is between 50 and 75 years of age. *Id.* First Matloubian Rep. at 6.

The parties agree that Petitioner was correctly diagnosed with seropositive anti-CCP-positive rheumatoid arthritis. Tr. at 10, 90.

B. *Althen* Prong One

Under *Althen's* first prong, the causation theory must relate to the alleged injury. Petitioner must provide a "reputable" medical or scientific explanation, demonstrating that the vaccines received can cause the type of injury alleged. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). The theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). It must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioner is not the first to assert a causal relationship between the flu vaccine and RA in the Vaccine Program. My colleagues and I have consistently found that petitioners have failed to produce preponderant evidence that the flu vaccine can cause RA. *See, e.g., Clark v. Sec'y of Health & Hum. Servs.*, No. 17-1553V, 2023 WL 4897284 (Fed. Cl. Spec. Mstr. June 16, 2023) (concluding that the perfect storm theory espoused by petitioner's expert was not sound and reliable); *Moran v. Sec'y of Health & Hum. Servs.,* No. 16-538V, 2021 WL 4853544 (Fed. Cl. Spec. Mstr. Oct. 4, 2021) (determining that molecular mimicry was not a sound and reliable theory to explain how the flu vaccine can cause RA); *Tullio v. Sec'y of Health & Hum. Servs.*, No. 15-51V, 2019 WL 7580149 (Fed. Cl. Spec. Mstr. Dec. 19, 2019) (same), *mot. for rev. denied*, 149 Fed. Cl. 448 (2020); *Hock v. Sec'y of Health & Hum. Servs.,* No. 17-168V, 2020 WL 6392770 (Fed. Cl. Spec. Mstr. Sept. 30, 2020) (finding that Petitioner's causation theory lacked sufficient medical or scientific reliability).

1. Petitioner's Molecular Mimicry Theory is not Persuasive

The medical literature states that RA is a complex disease whose etiology remains unclear, but likely involves a variety of genetic and environmental factors. *See, e.g.,* Iain B. McInnes & Georg Schett, *The Pathogenesis of Rheumatoid Arthritis,* 365(23) NEW ENG. J. MED. 23 2205-19, 2205 (2011) (filed as Ex. A, Tab 1); Malmström at 14.

Petitioner's expert, Dr. Gowin, articulated her causal theory as follows:

> The initiating event for rheumatoid arthritis is thought to be due to the antigen (foreign substance) dependent activation of T lymphocytes. A single driving antigen has not been identified in all patients and it is likely that there may be several that can initiate rheumatoid arthritis in genetically susceptible individuals by the mechanism of molecular mimicry. The activation of the immune cascade causes ingrowth of blood vessels, recruitment of further immune cells that produce antibodies like the classic rheumatoid factor and anti-CCP and proliferation of the lining of the joint (synovium) that eventually causes damages to the cartilage.

First Gowin Rep. at 9. *See also* Tr. at 21-22 (Dr. Gowin briefly discussing molecular mimicry). Although Dr. Gowin mentions molecular mimicry, she does not describe how the process occurs in flu vaccine-RA cases with any specificity. In fact, she testified at trial that she is not able to

identify which antigen from the vaccine reacts to self, and that her theory was not even specific to the flu vaccine – that any vaccine, "especially any that's made in a similar fashion to the flu vaccine," could cause RA. Tr. at 55-56.

It is well established in the Vaccine Program that, while the theory of molecular mimicry is generally considered to have some validity, a Petitioner must do more than invoke "the magic words 'molecular mimicry'" in order to satisfy the requirements of *Althen* prong one. *McGuinness v. Sec'y of Health & Hum. Servs.*, No. 17-0954V, 2021 WL 5292343, at *17 (Fed. Cl. Spec. Mstr. Oct. 20, 2021) (citing *McKown v. Sec'y of Health & Hum. Servs.*, No 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019)). Here, Dr. Gowin mentions molecular mimicry as a component of her causal theory but she provides no further explanation. I recognize that petitioners are not required to demonstrate a specific biologic mechanism which caused their disease, nor are they required to present medical literature or epidemiological studies in support of their theory. *See Kottenstette v. Sec'y of Health & Hum. Servs.*, 861 Fed. Appx. 433, 44-41 (Fed. Cir. 2021) (citing *Knudsen*, 35 F.3d at 549) (reaffirming the principle that "proof of causation does not 'require identification and proof of specific biological mechanisms[.]'"); *Andreu,* 569 F.3d at 1378-79. However, a petitioner's prong one theory must be reliable. The mere mention of molecular mimicry, without more, does not constitute a reliable or persuasive prong one theory.

I note that in *Moran v. Secretary of Health and Human Services*, I previously considered whether the flu vaccine can cause RA via molecular mimicry. *Moran v. Sec'y of Health & Hum. Servs.*, No. 16-538V, 2021 WL 4853544 (Fed. Cl. Spec. Mstr. Oct. 4, 2021). I did not find that theory persuasive in *Moran*, and similarly do not find it to be so here.

In addition to the fact that Dr. Gowin has done little more than invoke the words "molecular mimicry," other evidence suggests that the flu vaccine does not cause RA via molecular mimicry. First, as Dr. Matloubian noted, evidence does not support that the flu *virus* causes RA. Tr. at 97, 98. Dr. Gowin agreed. Tr. at 50-51. *See also*, Bruck et al., *Transient oligoarthritis of the lower extremity following influenza B virus infection: Case report*, 8 PEDIATRIC RHEUMATOLOGY 4, 1-3 (2010) (filed as Ex. 23) (noting that "arthritis associated with influenza virus infection in humans has, to our knowledge, not been documented in the international literature…"). Schattner states that in order for a viral vaccine to be established as a cause of autoimmunity, the viral infection should also be liked to autoimmunity. Ami Schattner, *Consequence or coincidence? The occurrence, pathogenesis, and significance of autoimmune manifestations after viral vaccines*, 23 VACCINE 3876-86, 3881 (2005) (filed as Ex. A, Tab 21) (hereinafter "Schattner"); *see also*, Noel R. Rose, *Negative selection, epitope mimicry and autoimmunity*, 49 CURRENT OPINION IN IMMUNOLOGY 51-55 (2017) (filed as Ex. A, Tab 24). According to Dr. Matloubian, "it's illogical to conclude that the influenza vaccine, which has the same antigen as the virus itself, can lead to rheumatoid arthritis through molecular mimicry." Tr. at 100. Dr. Gowin did not persuasively explain why the flu vaccine would cause RA while the flu virus has not been shown to do so. *See id.* at 67.[12]

[12] Indeed, Dr. Gowin testified that vaccines are different from viruses because they use adjuvants and modify pieces of the virus. Tr. at 67. In fact, Petitioner has not demonstrated that the flu vaccine administered in this case (Fluarix Quadrivalent) contains an adjuvant or that the proteins in the vaccine are modified. *See Id.* at 109 (Dr. Matloubian testifying that "as far as I know, the proteins are not modified in

The Malmström article, which discusses the pathogenesis of RA, describes antigens from influenza virus as an "unrelated antigen" and uses it as a negative control in the study. Malmström at 7. Dr. Matloubian described this as "a strong indicator that the general medical and research communities that study pathogenesis of RA do not recognize any relationship between RA associated antigens and those of influenza virus." First Matloubian Rep. at 14. This point constitutes persuasive evidence which further undermines Petitioner's position that the flu vaccine caused Petitioner to develop RA via molecular mimicry.

2. The Remainder of Petitioner's Causal Theory is not Persuasive

The remainder of Petitioner's causal theory is nondescript. Dr. Gowin references immune complexes and immune cascade. First Gowin Rep. at 9; Tr. at 23. She testified as follows:

> So immune complexes -- the best way to kind of think about immune complexes is that the antibodies are these Y-shaped things which you can see in the cartoon. The different parts of that Y have different charges on them, so things will attract or repel to those charges. So you can think of them almost like magnets. Right?
>
> So -- and if you get a whole bunch of antibodies together and put them in a pile, it'd be like putting a little pile of Y-shaped magnets together, and those would form clumps, and that would be kind of what an immune complex is, and it can -- there can actually be other things that attach on to those -- to the charges.
>
> And then those immune complexes can either be big enough that they clog things up like your blood vessels, or your immune system recognizes that that big clump of things isn't normal, and it starts to attack those immune complexes.

Tr. at 23. Dr. Gowin testified that each of these mechanisms works in concert to result in RA. *Id.* at 25. Dr. Matloubian persuasively opined that immune complex formation would be more likely after influenza infection than after vaccination because there are a lot more antigens made during an infection than after a vaccine. Tr. at 118. The fact that there has been no demonstrated association between viral infection and RA strongly undermines Dr. Gowin's theory. Ultimately, I find Dr. Matloubian's testimony regarding immune complexes to be far more persuasive than that of Dr. Gowin.[13]

3. The Majority of Persuasive Studies do not Support a Connection between Flu Vaccine and RA

Several large studies have been performed to assess whether the flu vaccine causes RA. Each study indicates that there is not an association between the two.

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influenza vaccine"); *see also*, CDC, *Vaccine Safety, Adjuvants and Vaccines*; www.cdc.gov/vaccinesafety/concerns/adjuvants.html (last visited Dec. 6, 2023) (noting that the influenza vaccine does not contain an adjuvant except for the Fluad and Fluad quadrivalent vaccines).

[13] This is due, in part, to the fact that Dr. Matloubian has a Ph.D. in virology/immunology.

Epidemiologic evidence is relevant with respect to *Althen* prong one. *See, e.g., D'Tiole v. Sec'y of Health & Hum. Servs.,* 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review den'd*, 132 Fed. Cl. 421 (2017), *aff'd*, 726 Fed. Appx. 809 (Fed. Cir. 2018); *Blackburn v. Sec'y of Health & Hum. Servs.*, No. 10–410V, 2015 WL 425935, at *28–30 (Fed. Cl. Spec. Mstr. Jan. 9, 2015). However, this type of evidence is not required in order for a petitioner to establish that a vaccine can cause an injury. A vaccine injury is a rare event that cannot be disproved because a vaccinee did not experience a response consistent with that of the general population. *See Harris v. Sec'y of Health & Hum. Servs.*, No. 10–322V, 2014 WL 3159377, at *11 (Fed. Cl. Spec. Mstr. June 10, 2014) (finding that epidemiologic studies cannot absolutely refute causal connections, because it is possible that a larger study could always detect an increased risk).

In support of his position that Petitioner's RA was not caused by the flu vaccine, Dr. Matloubian discussed Ray. First Matloubian Rep. at 10 (citing Paula Ray et al., *Risk of rheumatoid arthritis following vaccination with tetanus, influenza and hepatitis B vaccines among persons 15-59 years of age*, 29 VACCINE 6592-97 (2011) (filed as Ex. 15, Tab F) (hereinafter "Ray"). This study involved a medical chart review of approximately one million patients in the Kaiser Permanente system from 1997 through 1999 and included both a cohort analysis and a case-control analysis. Ray at 6592. In Ray, the cohort analysis found a possible association between the flu vaccine and RA in windows approximately six months and one year after flu vaccination. *Id.* at 6596. The researchers in Ray then conducted a larger case-control analysis which concluded that there was no additional risk of developing RA after flu vaccination. *Id*.

Dr. Gowin testified that Ray found an increased relative risk for RA in the 180 and 365 day timeframes. Tr. at 20; Ray at 6594, table 3. She further opined that the researchers did a poor job of matching the cases and controls when they performed the case control study; for example, there were a lot more men in the control group and men are less likely to develop RA than women. As a result, she opined that it is difficult to know how to interpret the case control study. Tr. at 19-20. Dr. Matloubian persuasively testified that Ray's initial finding, that there was an association between the flu vaccine and development of RA within 180 and 365 days does not comport with a molecular mimicry theory, which Dr. Gowin has agreed should develop within six weeks. I agree. Tr. at 126. Ray ultimately concluded that "A possible association between RA and influenza vaccination in the cohort study was not borne out in the larger case-control analysis." Ray at 6592. I find that the Ray study provides strong evidence that there is no association between flu vaccine and RA in support of a molecular mimicry theory.

Dr. Matloubian also referred to the Bengtsson case-control study. First Matloubian Rep. at 10 (citing Bengtsson). This study followed 1998 cases of RA and 2252 controls for five years after vaccination. Bengtsson at 1831. Bengtsson found no association between the development of RA and prior vaccine exposure. *Id.* at 1832. Significantly, Bengtsson also found no increased risk of developing RA after vaccination in subjects who were smokers or who were carriers of HLA-DRB1 SE, the two best known risk factors for RA. *Id.* I find that this study also provides persuasive evidence that flu vaccine is not associated with RA.

Dr. Matloubian cited Fomin, which assessed the safety of the flu vaccine in patients already diagnosed with RA based on data from 82 RA patients and 30 healthy controls. I. Fomin et al., 65 ANNALS OF RHEUMATIC DISEASES 191-94, 191 (2006) (filed as Ex. 15, Tab E) (hereinafter

"Fomin"). The authors of this study concluded that "[v]accination against influenza was not associated with a significant worsening of any clinical or laboratory index of disease activity." Fomin at 193. I find that the absence of evidence that flu vaccination exacerbates pre-existing RA supports Respondent's position that the flu vaccine does not cause RA. The authors of the Westra article came to the same conclusion in their review of the literature. This literature review reported on six studies which addressed the safety of the flu vaccine in patients with autoimmune rheumatic diseases, including RA. *Id.* at 140. The authors stated that "no significant influence of vaccination on disease activity has been reported." *Id*. Schattner came to the same conclusion in her literature review. Schattner at 3876 ("whenever controlled studies of autoimmunity following viral vaccines were undertaken, no evidence of an association was found."). In addition, Dr. Matloubian testified that the American College of Rheumatology concluded that the flu vaccine is recommended for people with RA. Tr. at 136; Singh at 17.

The totality of the literature submitted by Respondent persuasively demonstrates that there is not an association between the flu vaccine and RA.

Dr. Gowin submitted several medical articles in support of her position that the flu vaccine can cause RA. These papers, in their totality, and not persuasive. I have discussed several of them, below.

One such paper is Basra, a case report describing one woman who developed RA after H1N1 influenza vaccine. The authors note that "there is very little evidence in the literature for any association between swine influenza vaccination and RA." Basra at 2.

Dr. Gowin also cited Schur for the proposition that lymphocytes specific for the influenza virus have been found in the joints of patients with RA suggesting they are implicated in the onset and the flare of disease .[14] First Gowin Rep. at 9. Dr. Matloubian disagreed with this interpretation, opining that these lymphocytes do not play any role in the development of RA. Tr. at 109. He testified as follows:

> in chronic inflammation, there's formation of what's called tertiary lymphoid organs, and the reason they're called tertiary is that they're really not involved [in the] usual immune responses. They happen at sites of chronic inflammation, for example, in the synovium, in the joint in rheumatoid arthritis. … So it turns out that these tertiary lymphoid organs use chemokines to become highly organized and attract cells to come in there. And the reason they do that is that … they think there's an infection, and they want to bring other cells there. [These cells] come to the synovium. If there is no antigen that can activate their B cell receptor or the T cell receptor in case of the T cells, they don't contribute to the immune response there. They don't make any cytokines. They don't activate the immune system, so they are basically going through, checking it out, and eventually if there's nothing there, they will leave.

[14] Schur does not discuss this issue, instead it is described in a separate paper cited by Dr. Gowin (Iyngkaran et al., *Rheumatoid vasculitis following influenza vaccination*, 42 RHEUMATOLOGY 7, 907-09 (2003) (filed as Ex. 15, Tab C).

Tr. at 111-12. Dr. Matloubian testified that he was not at all surprised there would be T cells or B cells specific for influenza in the synovium of people with RA because "that's what memory T cells and B cells do." *Id.* at 113. He testified that these cells circulate at the site of inflammation, but it does not mean they become activated or contribute to the disease process. *Id.* Dr. Gowin did not respond to this testimony.

Dr. Gowin also cited to the Herron study where the authors noted that six out of 17 RA patients had disease flares after influenza vaccination. Herron at 55. Dr. Matloubian pointed out that Herron studied their entire patient group a second time; during this second evaluation, the authors saw seven flares out of 13 participants. Dr. Matloubian testified this supports the point that people with diseases like RA tend to have flares. Tr. at 132. This opinion is supported by the authors' conclusion that "[s]ince similar proportions of patients had flare-ups during both study periods, it seems unlikely that exacerbations during the first period could be attributed to vaccination." Herron at 55. This seems especially true given that the second evaluation occurred nearly five months after vaccination, too long for the immune response that is a central component of the autoimmune process in Petitioner's causal theory to be medically reasonable.

It is well established in the Vaccine Program that a petitioner is not required to provide epidemiological studies in order to satisfy prong one of the *Althen* analysis. *Capizzano*, 440 F.3d at 1325. Case reports can provide some limited support for a petitioner's theory of causation. *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. 650, 668 (2011) ("Case reports do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value compared particularly to formal epidemiological studies. Nonetheless, the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight."). Accordingly, I conclude that the case reports Petitioner filed do provide some support for her claim that the flu vaccine caused her RA. However, I find the epidemiological studies filed by Respondent more persuasive.

Ultimately, in evaluating the medical literature filed in this case, the weight of the evidence suggests that there is not an association between flu vaccine and RA. Although I have considered Petitioner's filings, I have credited the larger studies (Ray, Bengtsson, Fomin, and Westra) over the case reports and other literature filed by Petitioner.

Considering the totality of the evidence discussed above, I find that Petitioner has not presented a sound and reliable theory that preponderantly shows that the flu vaccine can cause RA. Petitioner has not satisfied the first *Althen* prong.

C. *Althen* Prong Two

Under *Althen's* second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Id.* A petitioner is not required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Id.* (omitting internal citations). *Capizzano*, 440 F.3d at 1325. Instead, circumstantial evidence and reliable medical opinions may

be sufficient to satisfy the second *Althen* prong.

1. Petitioner's Evidence

Dr. Gowin provided her opinion concerning the specific evidence in Petitioner's case that supported RA caused by the flu vaccine. She stated,

> A: Well, I -- you know, I think it obviously happened within a couple weeks in somebody who may have been predisposed to get it, and that was the second hit that was required for her to get clinical rheumatoid.
>
> Q: Is there anything else besides the temporal proximity?
>
> A: Other than just the knowledge that she's a [sic] background of someone who may get rheumatoid, I think it's -- other than the basic immunology theories of it, I -- the timing certainly fits in.

Tr. at 67-68.

Dr. Gowin has opined that Petitioner did not have RA before her flu vaccine, she developed RA after her flu vaccine, so the influenza vaccine *did cause* Petitioner's RA. The Federal Circuit in *Capizzano* noted that "[t]he second prong of the Althen ... test is not without meaning." *Capizzano*, 440 F.3d at 1327. Indeed, in *Althen*, the Court stated: "Although probative, neither a mere showing of a proximate temporal relationship between vaccination and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more, to meet the burden of showing actual causation." *Althen*, 418 F.3d at 1278.

2. Treating Physicians

In weighing evidence, special masters are expected to consider the views of treating doctors. *Capizzano*, 440 F.3d at 1326. The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. *See McCulloch v. Sec'y of Health & Hum. Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

In this case, no treating physician persuasively attributed Petitioner's RA to her flu vaccine. This is not surprising, as the cause of RA is unknown. I note that one of Petitioner's records states "She had a reaction to flu vaccine so we are wondering given she is in group [1-b] her reaction to potential covid vaccine." Ex. 30 at 378. Similarly, another record notes, "Does not get flu shot due to reaction." *Id.* at 2233. I do not find that these notes provide a persuasive connection between the flu vaccine and Petitioner's RA. In fact, they read more as a history provided by Petitioner rather than as a medical opinion.[15]

[15] Several other medical records discuss Petitioner's RA in the context of her vaccination, but none persuasively link her vaccination to her RA; indeed, these records do not discuss a causal relationship between the two. For example, a record from March 28, 2016, notes "all sx started October 2015 after flu

3. Petitioner Had a History of Smoking

Petitioner was a former smoker who smoked 0.8 packs of cigarettes per day from 1971 until 1986. Ex. 6 at 3.

Smoking is an established risk factor for RA. *See* Malmström at 2 (noting that smoking has a large impact on ACPA-positive patients); McInnes & Schett, (stating that "[s]moking and other forms of bronchial stress (e.g., exposure to silica) increase the risk of rheumatoid arthritis among persons with susceptibility HLA–DR4 alleles"); Laura Hunt & Paul Emery, *Defining populations at risk of rheumatoid arthritis: the first steps to prevention*, 10 RHEUMATOLOGY 521-30 (2014) (filed as Ex. A, Tab 6) (observing that smoking is a risk factor for seropositive RA). Although the risk decreases after smoking cessation, it does not reduce to zero. Tr. at 95.

Because smoking is a demonstrated risk factor for RA, it is more likely that this played a role in the development of Petitioner's disease rather than her flu vaccine. *See Stone v. Sec'y of Health & Hum. Servs.*, 676 F.3d 1373, 1379-80 (Fed. Cir. 2012) (finding that special masters can consider other possible sources of injury in making a determination under *Althen* prong two).[16]

For all these reasons, I conclude that Petitioner has not presented preponderant evidence in support of *Althen's* second prong.

D. *Althen* Prong Three

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, she must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013).

While there is little dispute that Petitioner developed RA several weeks after her October 13, 2015 flu vaccination, this fact standing alone is insufficient for Petitioner to meet her burden under *Althen* prong three. Because *Althen* prong three coincides with *Althen* prong one, Petitioner's inability to articulate a sound and reliable causal theory effectively precludes her from establishing a medically appropriate temporal interval between vaccination and the onset of disease. Even assuming that Petitioner had satisfied *Althen* prong three, that alone would not meet Petitioner's overall burden of proof. *Veryzer v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that a "temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury.").

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shot on 10/13/15…" Ex. 6 at 118. Another record from April 12, 2016, documents that "Judy reports onset of difficulties back in October after receiving a flu shot." Ex. 5 at 1003.

[16] I note that while smoking has been persuasively identified as an environmental trigger for RA, Respondent has not contended that smoking is an alternate cause of Petitioner's disease. Although I have considered Petitioner's history of smoking in my analysis, even without this evidence, I would have found Petitioner's prong two showing to have been deficient for the reasons articulated in this decision.

Because of this, Petitioner has not presented preponderant evidence with respect to the third *Althen* prong.

VII. CONCLUSION

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, medical literature, the affidavits, as well as the experts' opinions and testimony, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. **Her petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[17]

IT IS SO ORDERED.

s/ Katherine E. Oler
Katherine E. Oler
Special Master

[17] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.